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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
UNGAR, SUSAN NMN	
ART UNIT	**PAPER NUMBER**
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/696,487	BUCHHOLZ ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *30 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *4-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. The Amendment filed April 30, 2007 in response to the Office Action of February 6, 2007 is acknowledged and has been entered. Previously pending claims 1-3 have been amended. Claims 1-3 are currently being examined.

2. Applicant states that the foreign document to which priority is claimed is related to the instant invention. Applicant will investigate and if found necessary will submit a correct certified copy. The statement has is acknowledged and the priority date established by Examiner remains.

3. The following rejections are being maintained:

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 1 remains rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed February 6, 2007, Section 6, pages 3-7.

Applicant argues that Examiner has not present an argument that the claimed method is not enabled when the nucleic acid to be detected is one which encodes the amino acid sequence of SEQ ID NO:2.

The argument has been considered but has not been found persuasive because Applicant is arguing limitations not recited in the claims as currently constituted because the claims are not drawn to nucleic acid which encodes the amino acid sequence of SEQ ID NO:2, but rather are drawn to detecting mRNA encoding a polypeptide **having** (emphasis added and interpreted by the Office as comprising) the amino acid sequence of SEQ ID NO:2). Further, contrary to

Applicant's argument Examiner specifically stated that while enabling for a method of determining the presence or absence of pancreatic cancer in a patient comprising detecting SEQ ID NO:1, the specification does not reasonably provide enablement for determining the presence or absence of pancreatic cancer comprising detecting an amount of nucleic acid encoding UKW, wherein Examiner specifically pointed to the single example, disclosed in the specification, of the relative expression of SEQ ID NO:1 compared to a control and the teaching that this mRNA is a target for specific diagnosis of pancreatic cancer, wherein Examiner specifically stated that "one cannot extrapolate the teaching of the specification to the scope of the claims because the claims are drawn to a whole universe of nucleic acids encoding undefined UKW, wherein it cannot be predicted that any UKW other than SEQ ID NO:1 is in fact in any way associated with pancreatic cancer. Although the claim is now drawn to detecting an mRNA encoding a polypeptide comprising SEQ ID NO:2, the issue remains the same, that is, there is no teaching in either the specification or the art or record that any mRNA other than that which is useful to produce the cDNA consisting of SEQ ID NO:1, is in any way associated with pancreatic cancer.

Applicant's arguments have not been found persuasive and the rejection is maintained.

6. Claim 1 remains rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed February 6, 2007, Section 7, pages 7-11.

Applicant argues that the definition of the nucleic acid as being one that encodes a polypeptide having the amino acid sequence of SEQ ID NO:2 constitutes a relevant identifying characteristic since the structure of the nucleic acid must be such that it encodes the amino acid sequence of SEQ ID NO:2 and

that this constitutes a precise definition of the claimed subject matter and one of skill in the art would know exactly which codons are necessary to encode such a sequence and that there is a limited number of nucleic acids that can encode such a sequence and that this constitutes a precise definition under the standard set in Lilly. The argument has been considered but has not been found persuasive because the term "having" in the phrase "having the amino acid sequence of SEQ ID NO:2" is read as comprising and one could clearly not know which codons are necessary to encode the structure as currently claimed (see the rejection under 35 USC 112, first paragraph written description below). Further, although the number of nucleic acids encoding the polypeptide consisting of SEQ ID NO:2 is clearly limited, the number of mRNA is still drawn to a whole universe of molecules given the known degeneracy of the code and the fact that SEQ ID NO:2 consists of 373 amino acids. Thus, the number of possible permutations and combinations of codons/degenerate codons is greater than the number of stars in the universe. Further, although one might know that there is a limited number of mRNA that would encode a polypeptide consisting of SEQ ID NO:2, the specification provides no information that would satisfy either the Lilly or the Enzo standards drawn to that mRNA that would encode polypeptide consisting of SEQ ID NO:2 that is useful for determining the presence or absence of pancreatic cancer in a patient given that only a single example, SEQ ID NO:1 has been disclosed in the specification, given that the specification provides no functional characteristics coupled with a known or disclosed correlation between the structure and function of the broadly claimed genus of mRNA.

Finally, Applicant argues that as the level of such nucleic acid is increased in pancreatic cancer cells, the level of such nucleic acid is useful for determining the

presence or absence of pancreatic cancer. The argument has been considered but has not been found persuasive because the written description requirement is separable from the enablement requirement and thus this argument is moot as drawn to the written description requirement. Further, as set forth previously and above, only a single nucleic acid useful for determining the presence or absence of pancreatic cancer has been taught by the specification and this is not sufficient to provide a written description of the broadly claimed invention.

7. Claims 2 and 3 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed February 6, 2007, Section 8, pages 11-14.

Applicant argues that Examiner's interpretation of the '143 patent is incorrect and that the term "complementarity" is distinguishable from the term "complement" and argues that "if the term "complementary" would be broad enough to include partially complementary nucleic acid sequences as well as those that are completely complementary, then there would be no need to use the modifier 'partial". The argument has been considered but has not been found persuasive because as understood by those of ordinary skill in the art, inferred by and inherent to the term "complementarity" is that the term is drawn to complements of nucleic acid species. Further, as previously set forth the reference specifically teaches that those of ordinary skill in the art interpret the term "complementarity to encompass both partial and complete complements", thus Applicant is correct there is no need to use the modifier term "partial" because those of ordinary skill in the art recognize that the term encompasses partial complements. Although Applicant states that "in view of the correct definition of complementary", the claims are enabled, the argument has been considered but has

not been found persuasive because Applicant has not submitted or disclosed objective evidence, or writings of those of ordinary skill in the art defining the term "complementary" or submitted objective evidence that teaches that the term "complementary" is limited to complete complements.

Applicant argues that Examiner has not presented an argument that the claimed method is not enabled when the probe is complementary (as the term is correctly defined) to SEQ ID NO:1 or a fragment thereof. The argument has been considered but has not been found persuasive because, in the absence of a limiting definition in the specification, in the absence of objective evidence from those of skill, the definition of complementary set forth in the action is reasonable and correctly defined and for the reasons of record, the claims are not enabled.

Applicant argues that, as drawn to claim 2, that the claim recites a step in which the level of hybridization present between the probe and nucleic acids in a test sample is compared with the level of hybridization between the probe and nucleic acids in a sample that is known not to contain pancreatic tumor cells, wherein paragraph 0044 of the specification states that an approximately 15-fold increased amount of UKW gene in a test sample in comparison with the respective amount in a control sample would be indication that the test sample contains pancreatic tumor cells and as such the specification clearly shows how one skilled in the art would determine whether the test sample contains pancreatic cancer cells or fluid thereform.

The argument has been considered but has not been found persuasive because Applicant is arguing limitations not recited in the claims as currently constituted, the claims are not drawn to the probe with which the approximately 15-fold increase was found, rather, a review of the specification reveals that the

scope of the claim is not enabled because the assays exemplified are not conducted with probes "complementary" but rather the specification teaches that the assays are conducted only with probes that are 100% complementary to SEQ ID NO:1 (see pages 16 and 17). This is not sufficient to enable the broadly claimed invention.

Applicant argues that, as drawn to claim 3, that the claim has been amended to include the step of comparing the levels of UKW mRNA as demonstrated by the level of hybridization, with the levels of mRNA for a housekeeping gene. Applicant points to the specification wherein there is at least 3-fold greater amount of UKW mRNA than mRNA of a housekeeping gene.

The argument has been considered but has not been found persuasive because a review of the specification reveals that the scope of the claim is not enabled because the assays exemplified are not conducted with probes "complementary" but rather the specification teaches that the assays are conducted only with probes that are 100% complementary to SEQ ID NO:1 (see pages 16 and 17). This is not sufficient to enable the broadly claimed invention.

It is noted that, although claims 2 and 3 have now been amended to recite specific hybridization conditions and Applicant has not presented arguments drawn to the newly recited hybridization conditions, the newly added hybridization conditions do not enable the scope of the claims because the specification teaches that the hybridization conditions are "moderate conditions" (see para 0039 of the published application) and therefore the claims still read on a whole universe of detected molecules.

8. Claims 2 and 3 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed February 6, 2007, Section 9, pages 14-18.

Applicant argues that amendment of the claims to recite specific hybridization conditions obviates the rejection under the written description requirements of 35 USC 112, first paragraph. The argument has been considered but has not been found persuasive because the hybridization conditions claimed are moderate conditions as defined by the specification (see para 0039) and the claims still read on a whole universe of molecules for the reasons set forth previously and above and the stated conditions do not provide a written description or meet the standards of either Lilly or Enzo for the reasons of record.

Applicant reiterates arguments that Examiner has misinterpreted the meaning of complementary and that given Applicant's opinion of what complementary means, the specification as originally filed contains a written description of the claimed invention. The argument has been considered above and has not been found persuasive for the reasons set forth above.

9. Claims 2 and 3 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed February 6, 2007, Section 10, pages 18-20.

Because it appears that Applicant has not distinctly and specifically point out the supposed errors in the rejection, the rejection is maintained.

10. Claim 2 remains rejected under 35 USC 112, second paragraph for the reasons previously set forth in the paper mailed February 6, 2007, Section 12, page 22.

Applicant argues that the claims are to be read in the light of the specification and the specification clearly states that an approximately 15-fold increased amount of UKW mRNA in a test sample would be an indication that the test sample contains pancreatic tumor cells. The argument has been considered but has not been found persuasive because Applicant is reminded that although the claims are interpreted in light of the specification, limitations recited in the specification are not read into the claims.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

11. Claim 1 is are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of detecting mRNA encoding a polypeptide having the amino acid sequence of SEQ ID NO:2 claimed in Claim 1, which is interpreted by the office as detecting mRNA encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:2, has no clear support in the specification and the claims as originally filed. In the response filed April 30, 2007, Applicant points to support for the newly added limitation in the application at paragraph 0036. A review of paragraph 0036 reveals support for;

> [0036] According to the invention there are provided methods for identifying and isolating of UKW antagonists which have utility in the treatment of cancer. These methods include methods for modulating the expression of the polypeptides according to the invention, methods for identifying UKW antagonists which can selectively bind to the proteins according to the invention, and methods of identifying UKW antagonists which can modulate the activity of said polypeptides. The methods further include methods for modulating, preferably inhibiting, the transcription of UKW gene to mRNA. These methods can be conducted in vitro or in vivo and may make use of and establish cell lines and transgenic animal models

Of the invention.

Further, a review of paragraph 0036 in the published application reveals support for;

> [0036] As used herein, the term "UKW" means a nucleic acid encoding a polypeptide of SEQ ID NO:2, preferably the DNA sequence and the related mRNA sequence of SEQ ID NO:1 as well as the encoded polypeptide of SEQ ID NO:2. As UKW is a transmembrane receptor protein, the polypeptide is of outstanding interest for diagnosis and as an epitope for antibody binding the extracellular domain of UKW polypeptide is preferred. Therefore, it is preferred to direct the nucleic acid sample and probes to this region and especially to parts thereof which have low homology with other genes and polypeptides.

The suggested support has been considered but has not been found persuasive because nowhere in either paragraph 0036 of the specification as originally filed or in paragraph 0036 of the published application is there support for determining the presence or absence of pancreatic cancer comprising detecting mRNA that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2.
The subject matter claimed in claim 1 broadens the scope of the invention as originally disclosed in the specification.

12. Claim 1 is rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification or reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to a method requiring an mRNA encoding a polypeptide having (therefore comprising) the amino acid sequence of SEQ ID NO:2 which is useful for determining the presence or absence of pancreatic cancer. Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co.,

119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that A[a] written description of an invention involving a chemical genus, like a description of a chemical species, >requires a precise definition, such as by structure, formula, [or] chemical name,= of the claimed subject matter sufficient to distinguish it from other materials.≅ Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as Avertebrate insulin cDNA or Amammalian insulin cDNA without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that Anaming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. AA description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features

common to the members of the genus, which features constitute a substantial portion of the genus. Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that Athe written description requirement can be met by >show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. ≅ Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of an mRNA encoding a polypeptide having (therefore comprising) the amino acid sequence of SEQ ID NO:2 which is useful for determining the presence or absence of pancreatic cancer, per Lilly by structurally describing a representative number of mRNA encoding a polypeptide having (therefore comprising) the amino acid sequence of SEQ ID NO:2 which is useful for determining the presence or absence of pancreatic cancer or by describing structural features common to the members of the genus, which features constitute a substantial portion of the genus.

Alternatively, per Enzo, the specification can show that the claimed invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

In this case, the specification does not describe an mRNA encoding a polypeptide having (therefore comprising) the amino acid sequence of SEQ ID NO:2 which is useful for determining the presence or absence of pancreatic cancer in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any mRNA encoding a polypeptide having (therefore comprising) the amino acid sequence of SEQ ID NO:2 which is useful for determining the presence or absence of pancreatic cancer nor does the specification provide any partial structure of such mRNA, nor any physical or chemical characteristics of the mRNA receptor nor any functional characteristics coupled with a known or disclosed correlation between structure and function other than SEQ ID NO:1, synthesized by RT-PCR from the mRNA that encodes SEQ ID NO:2. Although the specification discloses a single representative molecule, this does not provide a description of an mRNA encoding a polypeptide having (therefore comprising) the amino acid sequence of SEQ ID NO:2 which is useful for determining the presence or absence of pancreatic cancer that would satisfy the standard set out in Enzo.

The specification also fails to describe an mRNA encoding a polypeptide having (therefore comprising) the amino acid sequence of SEQ ID NO:2 which is useful for determining the presence or absence of pancreatic cancer by the test set out in Lilly. The specification describes only a single molecule. Therefore, it

necessarily fails to describe a representative number of such species. In addition, the specification also does not describe Astructural features common to the members of the genus, which features constitute a substantial portion of the genus.

Thus, the specification does not provide an adequate written description of the broadly claimed mRNA that is required to practice the claimed invention or reasonably convey that the inventor(s) had possession of the invention at the time the application was filed. Since the specification fails to adequately describe the product critical to the claimed method, it also fails to adequately describe the claimed method and to convey to those of skilled in the art that the inventor(s) had possession of the invention at the time the application was filed.

13. Claim 2 is rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of detecting mRNA encoding a polypeptide having the amino acid sequence of SEQ ID NO:2 claimed in Claim 1, which is interpreted by the office as detecting mRNA encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:2, has no clear support in the specification and the claims as originally filed. In the response filed April 30, 2007, Applicant points to support for the newly added limitation in the application at paragraph 0039 and 0044. A review of paragraph 0039 reveals support for;

> [0039] "Nucleic acid probes and primers for UKW" as used herein means nucleic acid fragments useful for the detection of UKW nucleic acids by hybridization methods. Hybridization techniques and conditions are well-known to one skilled in the art. Such hybridization conditions are, for example, moderate stringent conditions including washing with a solution of 5.times.SSC, 0.5% SDS, 1.0 mmol/l EDTA, pH 8.0, followed by hybridization at 50-60.degree. C. 5.times.SSC overnight, washing at room temperature for 40 minutes with 2.times.SSC containing 0.1% SDS and afterwards washing with 0.1.times.SSC, 0.1% SDS at 50.degree. C. for 40

min with one change of fresh solution. It is also possible to use higher temperatures for hybridization (e.g. 65-70.degree. C.) as high stringent hybridization conditions. The nucleic acid probes and primers usually consist of a UKW nucleic acid segment of at least about 50 contiguous positions most preferably of 200 to 300 nucleotides The optimization of the probes and primers can be performed according to the state of the art. There exists informatic software (http://www-genome.wi.mit.edu/genom-e_software/other/primer3.html) which is generally used for such probe and primer design. For high selectivity it is preferred to use relatively low salt and/or high temperature conditions, for example, a salt concentration from about 0.02 mol/l to about 0.15 mol/l and temperatures of from about 50.degree. C. to about 70.degree. C.

Further, a review of paragraph 0044 reveals support for

[0044] As is shown in accordance with the present invention, the UKW nucleic acid is expressed in a greater amount in a pancreatic tumor sample than in a sample free from pancreatic_tumor cells and/or in a greater amount than a housekeeping gene. A test sample containing pancreatic tumor cells will have a greater amount of the UKW nucleic acid than does a sample which is free from pancreatic tumor cells. To identify a test sample as containing upregulated UKW nucleic acid, i.e., wherein the cells are pancreatic tumor cells or are tumor cells of a mammary carcinoma, it is preferable that the test sample have an approximate amount of UKW nucleic acid which is appreciably greater than the approximate amount in a sample free of pancreatic tumor cells. For example, a test sample having an upregulated UKW gene may have approximately 15- to approximately 60-fold increased amount of UKW gene than a sample free of pancreatic tumor cells or an at least 3-fold greater amount of UKW mRNA than mRNA of a housekeeping gene like glycerolaldehyde-3-phosphate dehydrogenase (GAPDH) or porphobilinogen deaminase.

The cited support has been considered but has not been found persuasive because, although drawn to UKW nucleic acids, the specification defines UKW nucleic acids as a nucleic acid encoding a polypeptide of SEQ ID NO:2, that is UKW is any nucleic acid encoding any polypeptide of SEQ ID NO:2, for example

2 amino acids of SEQ ID NO:2, there is neither contemplation for nor guidance in the cited support drawn to probes comprising 50 contiguous nucleotides of SEQ ID NO:1. The subject matter claimed in claim 2 broadens the scope of the invention as originally disclosed in the specification.

14. Claim 2 is rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of assaying a fluid from pancreatic tumor cells has no clear support in the specification and the claims as originally filed. In the response filed April 30, 2007, Applicant points to support for the newly added limitation in the application at paragraph 0039, paragraph 0043 and at paragraph 0044.

A review of paragraph 0039 reveals support for;

[0039] "Nucleic acid probes and primers for UKW" as used herein means nucleic acid fragments useful for the detection of UKW nucleic acids by hybridization methods. Hybridization techniques and conditions are well-known to one skilled in the art. Such hybridization conditions are, for example, moderate stringent conditions including washing with a solution of 5.times.SSC, 0.5% SDS, 1.0 mmol/l EDTA, pH 8.0, followed by hybridization at 50-60.degree. C. 5.times.SSC overnight, washing at room temperature for 40 minutes with 2.times.SSC containing 0.1% SDS and afterwards washing with 0.1.times.SSC, 0.1% SDS at 50.degree. C. for 40 min with one change of fresh solution. It is also possible to use higher temperatures for hybridization (e.g. 65-70.degree. C.) as high stringent hybridization conditions. The nucleic acid probes and primers usually consist of a UKW nucleic acid segment of at least about 50 contiguous positions most preferably of 200 to 300 nucleotides The optimization of the probes and primers can be performed according to the state of the art. There exists informatic software (http://www-genome.wi.mit.edu/genom-e_software/other/primer3.html) which is generally used for such probe and primer design. For high selectivity it is preferred to use relatively low salt and/or high temperature conditions, for example, a salt concentration from about 0.02 mol/l to about 0.15 mol/l and temperatures of from about 50.degree. C. to about 70.degree. C.

Further, a review of paragraph 0043 reveals support for;

[0043] In a further method according to the invention no second sample is used. For the detection whether the expression of UKW gene is upregulated, the level of mRNA of UKW is compared with the level of mRNA of a standard gene (housekeeping gene (see, e.g., Shaper, N. L., et al., J. Mammary Gland Biol. Neoplasia 3 (1998) 315-324; Wu, Y. Y., and Rees, J. L., Acta Derm. Venereol. 80 (2000) 2-3) of the cell, preferably by RT-PCR.

Further, a review of paragraph 0044 reveals support for;

[0044] As is shown in accordance with the present invention, the UKW nucleic acid is expressed in a greater amount in a pancreatic tumor sample than in a sample free from pancreatic_tumor cells and/or in a greater amount than a housekeeping gene. A test sample containing pancreatic tumor cells will have a greater amount of the UKW nucleic acid than does a sample which is free from pancreatic tumor cells. To identify a test sample as containing upregulated UKW nucleic acid, i.e., wherein the cells are pancreatic tumor cells or are tumor cells of a mammary carcinoma, it is preferable that the test sample have an approximate amount of UKW nucleic acid which is appreciably greater than the approximate amount in a sample free of pancreatic tumor cells. For example, a test sample having an upregulated UKW gene may have approximately 15- to approximately 60-fold increased amount of UKW gene than a sample free of pancreatic tumor cells or an at least 3-fold greater amount of UKW mRNA than mRNA of a housekeeping gene like glycerolaldehyde-3-phosphate dehydrogenase (GAPDH) or porphobilinogen deaminase.

The cited support has been considered but has not been found persuasive because, there is neither contemplation for nor guidance in the cited support drawn to assay of fluids derived from pancreatic tumor cells. The subject matter claimed in claim 3 broadens the scope of the invention as originally disclosed in the specification.

15. If Applicant were able to overcome the rejections set forth above, claim 3 would still be rejected under 35 USC 112, first paragraph because the specification, while enabling for the claimed method for detecting pancreatic tumor comprising comparing the claimed mRNA from the test sample of patient suspected of having cancer to a second sample originating from non tumor pancreatic cell does not reasonably provide enablement for said method comprising comparing the claimed mRNA from said patient to a housekeeping gene to determine whether pancreatic cancer is present. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The specification teaches that "as is shown in accordance with the present invention, the UKW nucleic acid is expressed in a greater amount in a pancreatic tumor sample than in a sample free from pancreatic tumor cells and/or in a greater amount than a housekeeping gene. A test sample containing pancreatic tumor cells will have a greater amount of the UKW nucleic acid than does a sample which is free from pancreatic tumor cells. To identify a test sample as containing upregulated UKW nucleic acid, i.e., wherein the cells are pancreatic tumor cells or are tumor cells of a mammary carcinoma, it is preferable that the test sample have an approximate amount of UKW nucleic acid which is appreciably greater than the approximate amount in a sample free of pancreatic tumor cells. For example, a test sample having an upregulated UKW gene may have approximately 15- to approximately 60-fold increased amount of UKW gene than a sample free of pancreatic tumor cells or an at least 3-fold greater amount of UKW mRNA than mRNA of a housekeeping gene like glycerolaldehyde-3-phosphate dehydrogenase

(GAPDH) or porphobilinogen deaminase." paragraph 0044 of the published application. The specification further teaches at paragraph 0081 of the published application that "Real-time quantitative PCRs were performed with the TaqMan.RTM. technology and the ABI PRISM 7700 apparatus (Applied Biosystems, Foster City, Calif.). 10 .mu.g total RNA isolated from frozen adenocarcinomas of the pancreas, chronic pancreatitis and normal pancreatic tissues were used for reverse transcriptase reactions in a volume of 20 .mu.l. The PCRs were then carried out by mixing 200 ng cDNA with 4 .mu.l of 10.times.SYBR-Green buffer, 3 mM MgCl.sub.2, 1 mM dNTDs, 0.2 units Uracil-N Glycosylase, 1 unit AmpliTaq Gold, 4 .mu.l primer mix (300 nM each primer: forward 5'TTCTCTTTGACAGGTTCTGGGC3' (SEQ ID NO:3); reverse 5'GGTTGGAACCAGTAGGGCCTC3') (SEQ ID NO:4) in a final volume of 40 .mu.l. PCR primers were designed to generate a DNA fragment of 50 bp using the Primer Express Software (PE Biosystems, CA, USA). The amplification cycles were as follows: 2 min at 50.degree. C. followed by 10 min at 95.degree. C. and 40 amplification cycles (95.degree. C. for 15 sec and 60.degree. C. for 60 sec). These experiments were performed twice. The results were calculated by subtraction of gene UKW and housekeeping gene RNA steady-state levels for each sample. Each value was divided by the averaged steady-state level of UKW mRNA of three healthy tissues. Ratios were squared and a reciprocal value was formed."

One cannot extrapolate the teaching of the specification to the enablement of the scope of the claim because it is clear that the specification as originally filed presents contradictory information. Although the specification teaches that "the UKW nucleic acid is expressed in a greater amount in a pancreatic tumor sample than in a sample free from pancreatic tumor cells and/or in a greater amount than a

housekeeping gene" at paragraph 0044, the specification clearly discloses the actual practice of the invention wherein the specification clearly teaches that in the PCR studies disclosed not only tumor cells but also pancreatitis cells and **NORMAL** cells were assayed. In particular the specification teaches that "The results were calculated by subtraction of gene UKW and housekeeping gene RNA steady-state levels for each sample. Each value was divided by the averaged steady-state level of UKW mRNA of three healthy tissues. Thus it is clear that the claimed invention is not practiced with a comparison of mRNA of a housekeeping gene to that of the claimed mRNA in the absence of a comparison to a normal control in order to detect the presence of pancreatic tumor. Further no one of ordinary skill in the art would believe it more likely than not that one could differentiate any tumor from normal cell simply by comparing a tumor marker mRNA to a housekeeping gene from the same cell. In the absence of a comparison as disclosed by the specification at paragraph 0081, it could not be predicted, nor would it be expected that one could predictably distinguish between a tumor and normal cell based only on the assay as currently constituted thus it appears that whoever wrote the body of the specification did not understand the claimed invention

The specification provides insufficient guidance with regard to these issues d and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the claimed method would function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

16. Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is indefinite in the recitation of the phrase "greater level of hybridization" the claim is indefinite because the term "greater" is a relative term, it is not defined by the claim and the specification does not provide a standard for ascertaining the requisite degree and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

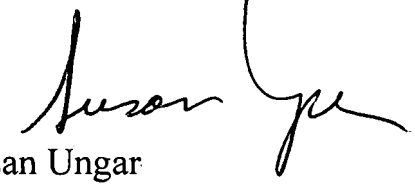
17. No claims allowed.

18. Applicant's amendment necessitated the new grounds of rejection. Thus, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley, can be reached at 571-272-0898. The fax phone number for this Art Unit is (571) 273-8300.



Susan Ungar
Primary Patent Examiner
July 2, 2007